# Registration accuracy of CT/MRI fusion for localisation of deep brain stimulation electrode position: an imaging study and systematic review

Geevarghese, Ruben ; O'Gorman Tuura, Ruth ; Lumsden, Daniel E ; Samuel, Michael ; Ashkan, Keyoumars

Abstract: BACKGROUND: Postoperative imaging is essential for verifying electrode location in patients undergoing deep brain stimulation (DBS). MRI offers better visualisation of brain targets, but concerns about adverse events have limited its use. Preoperative stereotactic MRI fused with a postoperative stereotactic CT, demonstrating the electrode position, is now widely used. OBJECTIVES: The aims of this study were to: (1) evaluate the accuracy of image registration using Neuroinspire, and (2) undertake a systematic review of the literature on CT/MRI fusion techniques to ascertain the accuracy of other software packages. METHODS: Twenty patients who underwent bilateral subthalamic nucleus DBS for Parkinson's disease were selected. The postoperative CT was registered and fused with the preoperative MRI using Neuroinspire. The position of each electrode tip was determined in stereotactic coordinates both in the (unfused) postoperative CT and the fused CT/MRI. The difference in tip position was used to evaluate the registration accuracy. RESULTS: The mean error ± SD of CT/MRI fusion using Neuroinspire was $0.25 \pm 0.15$, $0.33 \pm 0.26$ and $0.46 \pm 0.55$ mm in lateral, anteroposterior and vertical axes. A systematic review suggested that CT/MRI registration with Neuroinspire is more accurate than that achieved with other tested CT/MRI fusion algorithms. CONCLUSION: CT/MRI fusion for localisation of electrode placement offers an accurate, reliable and safe modality for assessing electrode location.

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# Registration Accuracy of CT/MRI Fusion for Localisation of Deep Brain Stimulation Electrode Position: An Imaging Study and Systematic Review

Ruben Geevarghese[a, b] Ruth O'Gorman Tuura[f] Daniel E. Lumsden[d]
Michael Samuel[c] Keyoumars Ashkan[b, e]

[a]Department of Neurosurgery, Charing Cross Hospital, Departments of [b]Neurosurgery and [c]Neurology King's College Hospital NHS Foundation Trust, King's Health Partners, [d]Complex Motor Disorders Service, Evelina Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, and [e]Clinical Neurosciences, Institute of Psychiatry, London, UK; [f]Department of MR Research, University Children's Hospital, Zurich, Switzerland

**Key Words**
Accuracy · CT · Deep brain stimulation · Electrode · Image registration · MRI · Review

**Abstract**
***Background:*** Postoperative imaging is essential for verifying electrode location in patients undergoing deep brain stimulation (DBS). MRI offers better visualisation of brain targets, but concerns about adverse events have limited its use. Preoperative stereotactic MRI fused with a postoperative stereotactic CT, demonstrating the electrode position, is now widely used. ***Objectives:*** The aims of this study were to: (1) evaluate the accuracy of image registration using Neuroinspire, and (2) undertake a systematic review of the literature on CT/MRI fusion techniques to ascertain the accuracy of other software packages. ***Methods:*** Twenty patients who underwent bilateral subthalamic nucleus DBS for Parkinson's disease were selected. The postoperative CT was registered and fused with the preoperative MRI using Neuroinspire. The position of each electrode tip was determined in stereotactic coordinates both in the (unfused) postoperative CT and the fused CT/MRI. The difference in tip position was used to evaluate the registration accuracy. ***Results:*** The mean error ± SD of CT/MRI fusion using Neuroinspire was 0.25 ± 0.15, 0.33 ± 0.26 and 0.46 ± 0.55 mm in lateral, anteroposterior and vertical axes. A systematic review suggested that CT/MRI registration with Neuroinspire is more accurate than that achieved with other tested CT/MRI fusion algorithms. ***Conclusion:*** CT/MRI fusion for localisation of electrode placement offers an accurate, reliable and safe modality for assessing electrode location. 

## Introduction

Parkinson's disease (PD) is a chronic degenerative movement disorder associated with bradykinesia, rigidity and resting tremor [1]. The mainstay of treatment is medical with pharmacological therapy aimed at increasing dopamine in the basal ganglia. The natural course of the disease results in a number of clinical challenges, including declining and fluctuating responses to medical therapy as well as medication-induced dyskinesia [2]. Deep brain stimulation (DBS) for PD is commonly considered in patients in whom there may exist one or more of the aforementioned challenges associated with progression of the disease [3].

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Prof. Keyoumars Ashkan, BA, BSc, MB, BCh, MRCP, FRCS, FRCP, FRCPS, FRCS (SN), MD
Department of Neurosurgery, Kings College Hospital
Denmark Hill, London SE5 9RS (UK)
E-Mail k.ashkan@nhs.net

DBS surgery is carried out with the aid of neuronavigational software to help direct electrode placement to the desired subcortical target. Confirmation of the satisfactory electrode placement is achieved through physiological, clinical and radiological parameters [4]. Radiologically, electrode localisation can be achieved through either MRI or CT [5]. There are advantages and disadvantages to both modalities with varying reported degrees of safety, accuracy and reliability.

CT assessment following electrode insertion offers a rapid, less expensive and freely available method for determining location. However, the comparatively low soft tissue contrast of CT (relative to that of MRI) affects the visibility of the target nuclei, and hence the extent to which electrode position can be determined relative to the target structures. Fusion of preoperative stereotactic MR images to stereotactic CT images after electrode insertion offers a combination of the advantages of the respective imaging modalities.

Previous reports have investigated the accuracy of software packages offering fusion of MR and CT images [6–8]. However, there is currently no data assessing the fusion accuracy of a new neuronavigational software package known as Neuroinspire (Renishaw plc, Wooton-under-Edge, UK). Additionally, there is an absence of recent review papers on the accuracy of CT/MRI fusion in DBS surgery despite a growing literature.

Hence, the aims of this study are twofold: firstly, to establish the fusion accuracy of CT/MRI using Neuroinspire, and, secondly, to undertake a systematic review of the literature on CT/MRI fusion techniques to ascertain the accuracy of other software packages.

## Methods

*Fusion Accuracy*

Overview

The protocol consisted of a preoperative stereotactic MRI and a postoperative stereotactic CT, both performed on the day of surgery for DBS electrode implantation. The postoperative CT is then fused with the preoperative MRI, enabling the position of the implanted electrode tip from CT to be visualised with respect to the DBS target structures on preoperative MRI. As the postoperative CT images are acquired stereotactically, this protocol allows for a quantitative, absolute assessment of the accuracy of the fused CT/MRI in comparison to the 'gold standard' stereotactic coordinates of the electrode tip from the postoperative (unfused) CT alone.

Subject Group

The subject group consisted of 20 retrospective patients referred for bilateral subthalamic DBS surgery for PD. All 20 patients had bilateral implants, resulting in a total of 40 implanted electrodes.

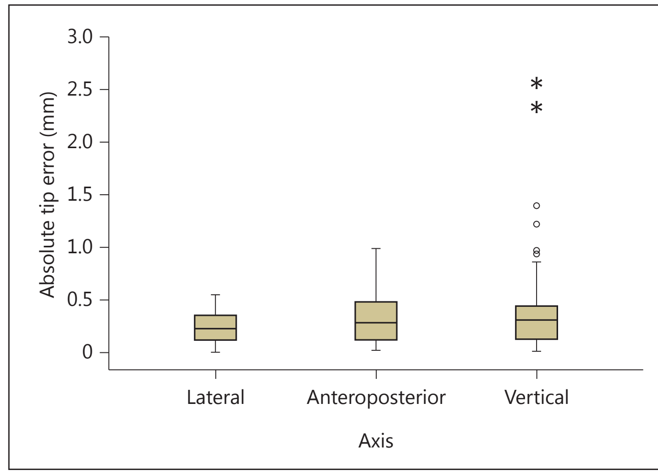


**Fig. 1.** Box-and-whisker plot of lateral, anteroposterior and vertical axis tip position error using Neuroinspire. Circles and asterisks indicate values between 1.5 and 3 times and more than 3 times the interquartile range, respectively.

Imaging

Preoperative stereotactic MRI was performed with a GE (General Electric) 1.5-tesla HD MRI scanner equipped with Twin-Speed gradients. For all patients, MRI was performed with Leksell G Frame (Elekta Instruments AB, Stockholm, Sweden). The MRI protocol included a $T_1$-weighted 3-dimensional inversion recovery prepared fast spoiled gradient echo volume, with inversion time = 450 ms, echo time (TE) = 3.5 ms, repetition time (TR) = 8.4 ms, flip angle = 25° and receiver bandwidth (BW) = ±23 kHz. The inversion recovery prepared spoiled gradient echo volume images were acquired with field of view = 240 mm, NEX = 1, matrix = 256 × 256 and slice thickness = 1.4 mm (subsequently resampled to 0.7 mm), resulting in a final voxel resolution of 0.94 × 0.94 × 0.7 $mm^3$.

Stereotactic targeting of the subthalamic nucleus was performed with a $T_2$-weighted fast spin echo (FSE), with TE = 91 ms, TR = 3 s, field of view = 240 mm, acquisition matrix = 256 × 256, BW = ±21 kHz, reconstruction matrix = 512 × 512, slice thickness = 2 mm, resulting in a final reconstructed voxel resolution of 0.5 × 0.5 × 2 $mm^3$.

Postoperative stereotactic CT imaging was performed with a GE LightSpeed CT scanner with 120 kV, 200 mA and 0.5 × 0.5 × 1.25 $mm^3$ resolution. Patients were scanned in the Leksell stereotactic G frame.

Registration Algorithm

The postoperative CT images were registered to the preoperative $T_1$-weighted MR images. The CT/MRI registration was performed with the Neuroinspire software package using a rigid body registration with 6 degrees of freedom (3 translations and 3 rotations), with normalized mutual information as the cost function. Registration for a single subject could be performed in 5–10 min.

Data Analysis

Image alignment was initially visually assessed to confirm that the registration had been successful (fig. 1). A quantitative assessment of


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**Table 1.** Results of clinical study and systematic review. 5 articles were identified which related to CT/MRI fusion in the context of intracranial electrodes

| Study | Imaging | Patients | Electrodes | Fusion algorithm/ software | x, mm | y, mm | z, mm | Geometric error |
|---|---|---|---|---|---|---|---|---|
| Barnaure et al. [5] | Pre- and post-operative MRI, postoperative CT | 23 | 46 | Integrated registration/AW VolumeShare, GE Healthcare | Left: 0.17±0.73<br>Right: 0.11±0.78 | Left: 0.97±0.96<br>Right: 0.73±0.86 | Left: 0.51±0.97<br>Right: 0.67±1.27 | Not reported |
| O'Gorman et al. [6] | Preoperative MRI and postoperative CT | 20 | 35 | Framelink v4.0<br>SPM: 1-step<br>SPM: 2-step<br>Vtkareg | 0.53±0.47<br>0.41±0.36<br>0.51±0.49<br>0.43±0.35 | 0.45±0.43<br>0.51±0.41<br>0.50±0.42<br>0.48±0.42 | 0.74±0.81<br>1.4±0.98<br>1.0±0.83<br>1.3±1.18 | 1.20±0.86<br>1.70±1.11<br>1.70±0.89<br>1.40±0.80 |
| Ferroli et al. [7] | Preoperative CT and postoperative MRI | 10 | 17 | Framelink v4.0 | 0.61±0.22 | 0.65±0.27 | 0.82±0.31 | Not reported |
| Thani et al. [8] | Intraoperative MRI and postoperative CT | 8 | 14 | Brainlab v2.6<br>Framelink v5.0 | 0.50±0.10<br>0.50±0.10 | 1.10±0.20<br>0.90±0.20 | 0.90±0.10<br>0.90±0.10 | 1.60±0.20<br>1.50±0.20 |
| Geevarghese et al. (this study) | Preoperative MRI and postoperative CT | 20 | 40 | Neuroinspire | 0.25±0.15 | 0.33±0.26 | 0.46±0.55 | 0.72±0.08 |

The results from these articles and our study are included with errors reported in the x-, y- and z-axes and additionally geometric error.

registration accuracy was achieved by evaluating the position of the electrode tip in stereotactic coordinates from both the unfused postoperative CT images (using the CT-visible fiducial markers) and the registered and fused CT/MRI (using the MRI-visible fiducial markers). The electrode tip was easily identified by following the track of the electrode from its point of entry until it disappeared.

As all measurements were calculated in stereotactic coordinates, the x-, y- and z-coordinates of the electrode tip derived from the postoperative unfused CT images could be directly compared to those of the fused CT/MR images to estimate the registration accuracy along each of the three spatial axes (x, y and z). The 3-dimensional difference in the position of the electrode tip in the fused images relative to that from the unfused postoperative CT images was then calculated.

A related-sample Friedman's two-way analysis of variance by ranks was used to assess if there was a significant difference in the distribution of lateral, anteroposterior and vertical registration errors. A value of $p < 0.05$ was deemed statistically significant.

### *Systematic Review*

#### Search Strategy

A systematic search of PubMed was conducted by 2 authors (R.G. and R.O'G.T.). Nine terms were searched; CT, computed tomography, MRI, magnetic resonance, fusion, registration, brain, head and electrode. The nine terms were connected through the Boolean operators 'OR' and 'AND' as follows: (CT OR 'computed tomography') AND (MRI OR 'magnetic resonance') AND (fusion OR registration) AND (brain OR head) AND (electrode).

#### Screen of Articles for Eligibility and Independent Review

Abstracts identified from the search were independently evaluated by the same 2 reviewers, and eligible articles were selected for full text review. During this initial screen, abstracts were considered only if they reported on original data (i.e. no review articles) and suggested to report on CT/MRI registration accuracy in the context of intracranial electrodes. Studies that looked at the difference between planned and actual electrode location were excluded, as this metric did not reflect the accuracy of the CT/MRI registration. Articles were then reviewed with the aim for data extraction, as described below.

#### Data Extraction

Studies were reviewed and the following data were extracted and included; number of patients, modality of imaging before and after electrode insertion imaging, number of electrodes, fusion accuracy in the x-, y- and z-directions, and geometric error.

## Results

### *Registration Accuracy*

The Neuroinspire algorithm demonstrated an accuracy of 0.25 ± 0.15 mm in the lateral, 0.33 ± 0.26 mm in the anteroposterior and 0.46 ± 0.55 mm in the vertical axes (absolute error ± SD). Geometric error was calculated as 0.72 ± 0.08 (mean ± SD). The findings are summarised in figure 1 and table 1.


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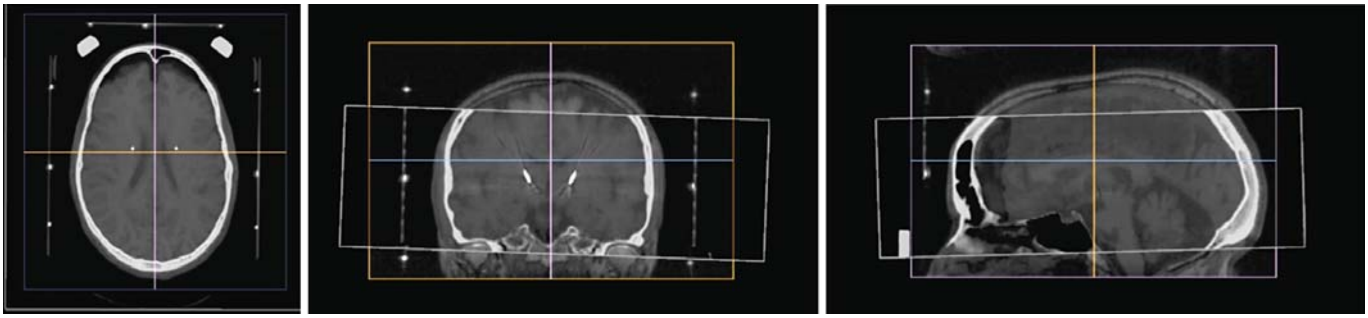

Color version available online

**Fig. 2.** Neuroinspire screenshot of a preoperative $T_1$ MR image fused to a CT image of the head after electrode insertion. Axial, coronal and sagittal views are demonstrated.

An example of a fused CT/MR image is included in figure 2. A post hoc related-sample Friedman's two-way analysis of variance by ranks showed a significant difference in the distribution of lateral, anteroposterior and vertical registration errors ($p < 0.001$). The errors in the x- and y-directions were not significantly different ($p = 0.11$, paired t test).

*Systematic Review*

Search Strategy and Independent Review

The search strategy identified 54 articles. Those which were identified from the abstract to suggest investigation of brain MRI/CT fusion accuracy were reviewed. Five articles reported brain MRI/CT fusion accuracy relating to electrode position. The data were extracted and are presented in table 1. From these previous studies reporting MRI/CR fusion accuracy, the mean orthogonal error in x, y and z was 0.42, 0.70 and 0.92 mm, respectively (ranges: x: 0.17–0.61 mm, y: 0.45–1.1 mm and z: 0.51–1.4 mm).

## Discussion

The Neuroinspire software package offers highly accurate registration and fusion of postoperative CT to preoperative MR images for patients undergoing DBS surgery for PD. Additionally, the results of the systematic review suggest that the accuracy of the Neuroinspire algorithm is comparable to or higher than previously reported with other software packages.

Optimal electrode position in patients undergoing subthalamic DBS is important in helping to reduce the risk of unwanted stimulation-related side effects. Adverse mood effects have been reported when stimulation is situated more ventrally [9] and stimulation of the oculomotor nucleus and resulting dysfunction in more medially sited electrodes [10]. The use of radiological evidence of electrode location through CT/MRI fusion may also help to reduce the incidence of such effects.

CT offers many advantages over MRI for postoperative imaging, including the lack of potential safety concerns with regard to heating of electrodes [11] and subsequent damage to surrounding brain tissue. This heating is thought to occur secondary to radiofrequency oscillating electromagnetic field excitation pulses applied to the DBS hardware circuit during scanning [12]. Whilst altering acquisition protocols and scanning under certain conditions may limit the risk of such heating effects, as indicated by a recent change in labelling by one of the DBS manufacturers [12, 13], the evidence base for general safe use remains limited. Postoperative CT with subsequent MRI fusion offers a comparatively safe method for DBS electrode localisation.

MRI following electrode insertion results in a signal void on the acquired images. The size of signal void is related to the sequence used for scan acquisition and particularly the choice of gradient echo versus spin echo- or FSE-based sequences, the echo time, pixel size and the readout BW [14]. One study compared the lead diameters seen on 2D FSE $T_2$, 3D FSE $T_2$, spin echo $T_1$ and magnetization prepared rapid acquisition gradient echo $T_1$ in postoperative DBS patients [15]. They reported mean lead diameters ranging from 2.1 to 4.0 mm, indicating that the signal void on MRI includes some tissue immediately surrounding the electrode in addition to the electrode itself. This large signal void adds a significant source of error to accurate localisation of electrode position with postoperative MRI in comparison to postoperative CT. CT additionally offers the potential for more rapid electrode localisation, as the postoperative CT scan may be acquired in under a minute while MR sequences for DBS localisation require a longer period of time for scan acquisition, on the order of 10 min [16].

We note from our post hoc analysis that there is a significant difference in reported x-, y- and z-axis errors seen in our imaging study, which appears to be due to the increased registration errors seen in the z-axis (0.46 ± 0.55 mm) compared to x-axis (0.25 ± 0.15 mm) and y-axis (0.33 ± 0.26) errors. The larger error in the z-(superior/inferior) direction is likely related to the larger slice thickness used in CT and MRI relative to the in-plane resolution in the x- and y-directions. In the present study, slice thicknesses of 1.5 and 1.25 mm were used for preoperative $T_1$ MRI and postoperative CT, respectively, although the MRI slices were subsequently interpolated to a slice thickness of 0.7 mm. The accuracy of CT/MRI fusion may, therefore, be improved through the reduction in slice thickness, although this may result in a reduction in the signal-to-noise ratio and/or a prolongation in scan acquisition time. Further investigation would, therefore, be necessary to clarify the source of the additional error observed in the z-(superior/inferior) direction.

Since structural MR images are subject to geometric distortion in the frequency-encoding direction, increased errors would be expected in the y-axis relative to the x-axis since the y-axis was used for frequency encoding in our MRI protocol. However, geometric distortion can be reduced by increasing the readout BW at the cost of increased image noise and a reduced signal-to-noise ratio. In our sample, using a BW of ±23 kHz, the x- and y-axis errors did not differ significantly (0.33 vs. 0.25 mm, $p = 0.11$, paired t test), but a trend towards increased error in the y-direction (the frequency-encoding direction) was observed, suggesting that subtle residual geometric distortion may be present despite the relatively high readout BW.

## Conclusions

We conclude that CT/MRI fusion offers an accurate, reliable and safe method for radiological localisation of DBS electrodes. Additionally, from our literature review, we note that Neuroinspire offers a highly accurate means to determine electrode position using this method.

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